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Case Report

Severe bilateral knee osteonecrosis in a young man with human immunodeficiency virus

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ABSTRACT

We present a young man with a background Human Immunodeficiency virus (HIV) who presented with bilateral knee pain and reduced mobility. Subsequent imaging of the knees demonstrated florid osteonecrosis (ON), which was managed conservatively. ON is seen more commonly in HIV patients than the general population, however the underlying mechanism for this association is remains unclear. An awareness of this disease is imperative to appropriately identify and manage such patients.

Introduction

This case highlights a significant comorbidity linked to human immunodeficiency virus (HIV) that is not regularly described and remains poorly understood. There are currently no guidelines or pathways to aid clinicians in the diagnosis and management of osteonecrosis (ON) in HIV patients, despite its increasing association. It is not clear whether the disease, pharmacological therapies or other factors cause the increase of ON in this population and therefore it is a challenging to prevent. However, timely identification of ON and referral to appropriate specialist care can have a positive impact on the patient outcomes.

Case presentation

A 29-year-old male with HIV presented to clinic with a 2-month history of increasingly severe, bilateral knee pain, as-

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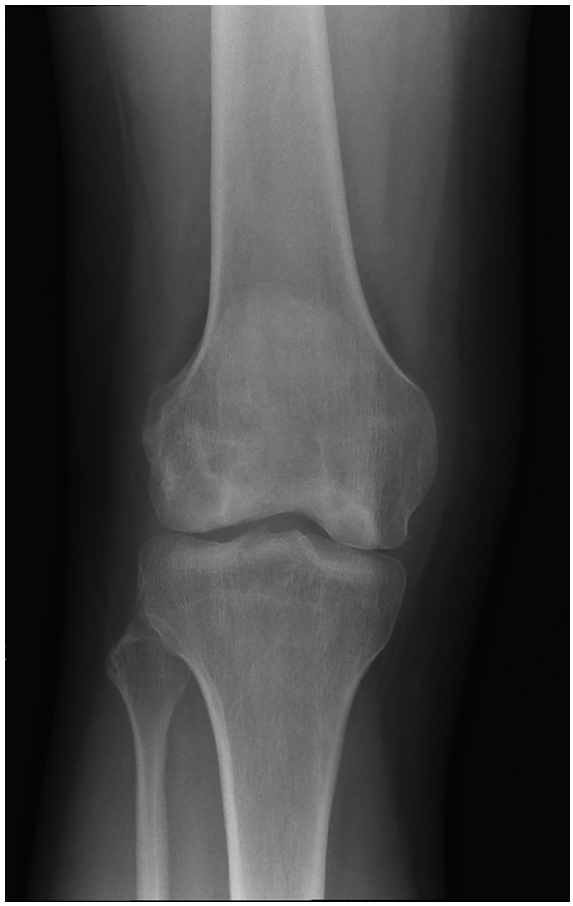

Fig. 1 – Anteroposterior (AP) x-ray view of the right knee demonstrating patchy sclerosis and increased lucency in the right medial and lateral femoral condyles.

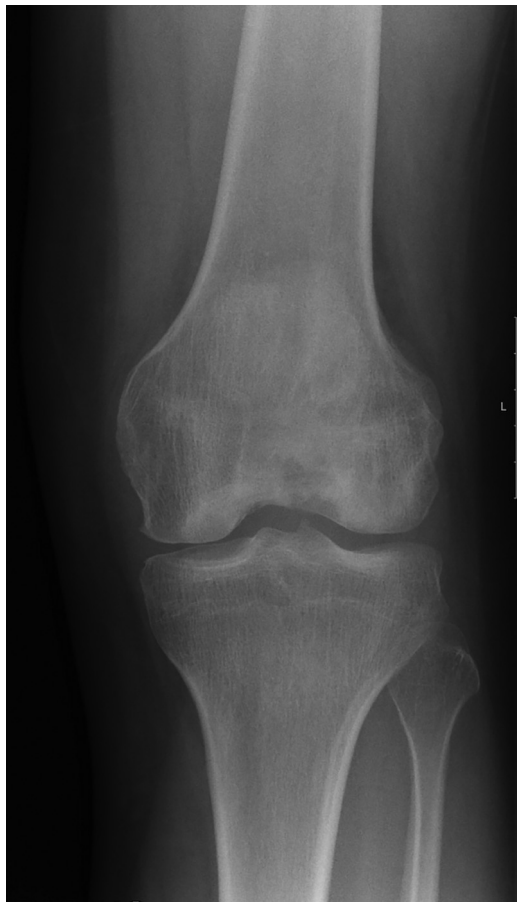

Fig. 2 – AP x-ray view of the left knee showing sclerosis and increased lucency within the medial aspect of the left lateral femoral condyle.

sociated with crepitus and swelling. He had been diagnosed with HIV 4 years previously following presentation with new onset confusion, a CD4 count of 10 (normal: > 400) and presumed cerebral toxoplasmosis on imaging. Since, he had suffered numerous comorbidities associated with HIV: cavitating pulmonary lesions; severe diarrhea and malnutrition requiring PEG feeding and osteoporosis, presumed to be secondary to antiretroviral therapy (ART). He had struggled with significant, intolerable side effects of many of the ARTs he was trialed on, which in total exceeded 10 different drugs, often necessitating novel combinations. A number of bisphosphonates were trialed but these too were not tolerated.

At the time of presentation with knee pain, blood tests demonstrated a low CD4 count of 191 and a viral load <20. Routine blood tests were normal, including serum calcium, phosphate, and cholesterol. Knee radiographs demonstrated patchy sclerosis and lucencies in the right medial and lateral femoral condyle and the left lateral femoral condyle (Figs. 1 and 2). Magnetic resonance imaging revealed multiple areas of bone infarction in the distal femora, proximal tibia and upper pole of the patellae with extensive bone marrow edema in the distal femur, sub-chondral collapse in the lateral femoral condyle, irregularity of the articular surface and ulceration (Figs. 3–6). A diagnosis of bilateral osteonecrosis was made.

The differential diagnoses in this presentation, based on the radiological findings, include primary disorders of the bone: osteoarthritis, osteochondritis dissecans, spontaneous osteonecrosis of the knee, and regional migratory osteoporosis. It also includes other systemic causes of osteonecrosis, such as sickle cell disease and systemic lupus erythematosus.

The patient was reviewed by orthopaedic colleagues who advised conservative management—knee supports and physiotherapy—suggesting arthroplasty and intra-articular injections would not be of benefit. Rheumatology and endocrinology input was sought and he is being monitored with DEXA scanning. He remains under the close supervision of the infectious diseases team who monitor, amongst his other comorbidities, his joint pain.

This patient continues to complain of bilateral knee pain that significantly limits his mobility. He has also complained of pain in other joints, including lumbar spine, wrists, and elbows; however, radiographs did not demonstrate ON at these sites. Recent repeat magnetic resonance imaging thankfully did not show any progression of the ON and his latest DEXA scan was stable.

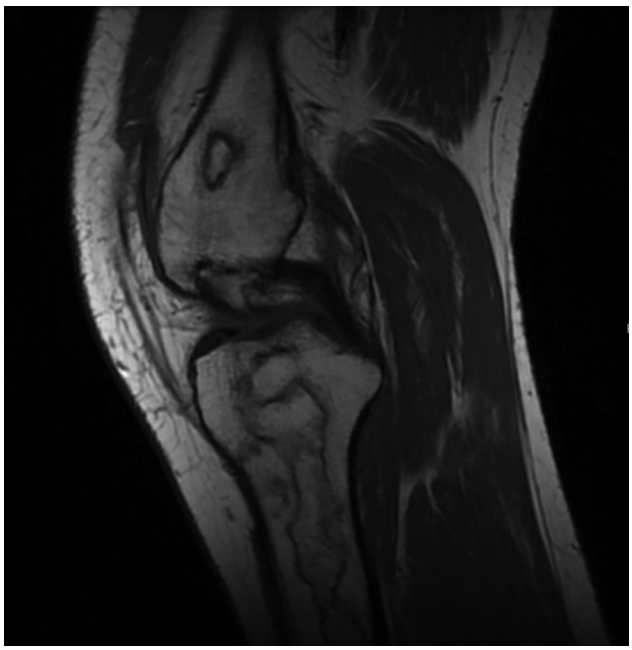

Fig. 3 – Sagittal T1W image of the right knee demonstrating multiple irregular serpiginous peripherally low signal abnormalities in the distal femoral metaphysis and proximal tibia in keeping with bone infarcts.

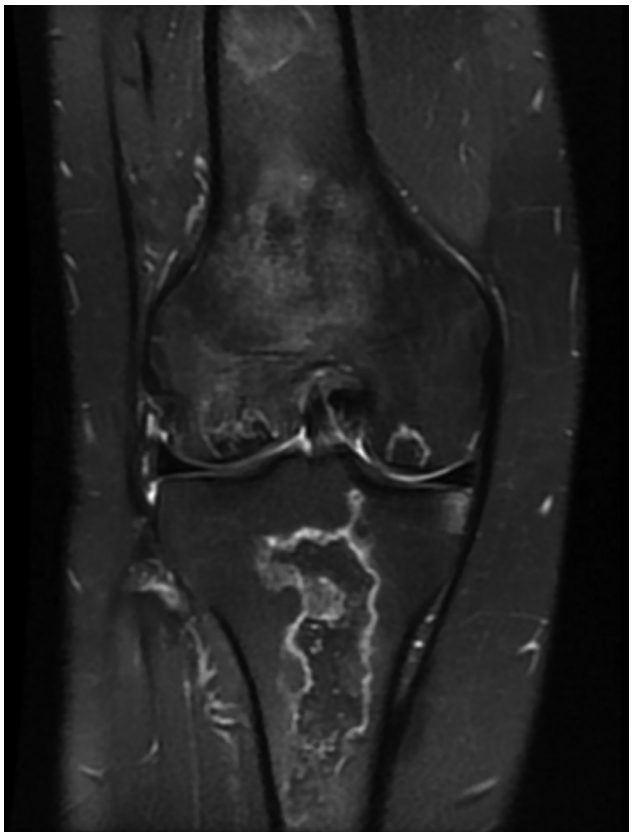

Fig. 4 – Coronal proton density fat saturated (PDFS) image of the right knee demonstrating involvement of the proximal tibia not seen on the corresponding x-ray (Fig. 1).

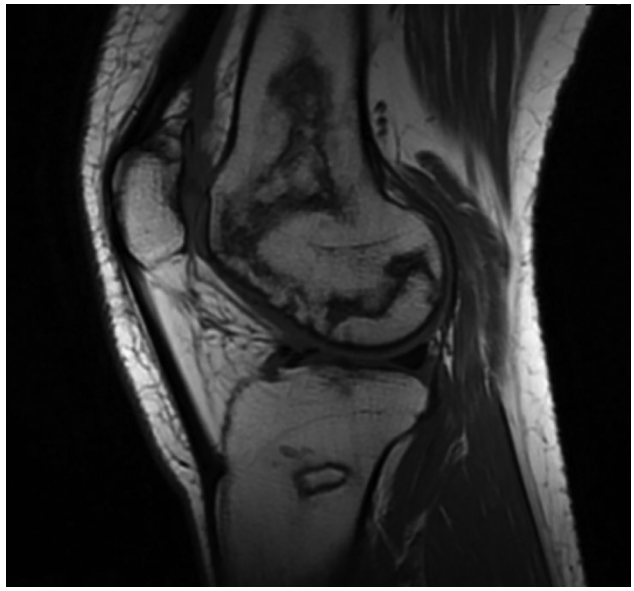

Fig. 5 – Sagittal T1W image of the left knee demonstrating similar changes to the contralateral side and subchondral collapse of the left lateral femoral condyle as well as irregularity of the articular surface and ulcerations.

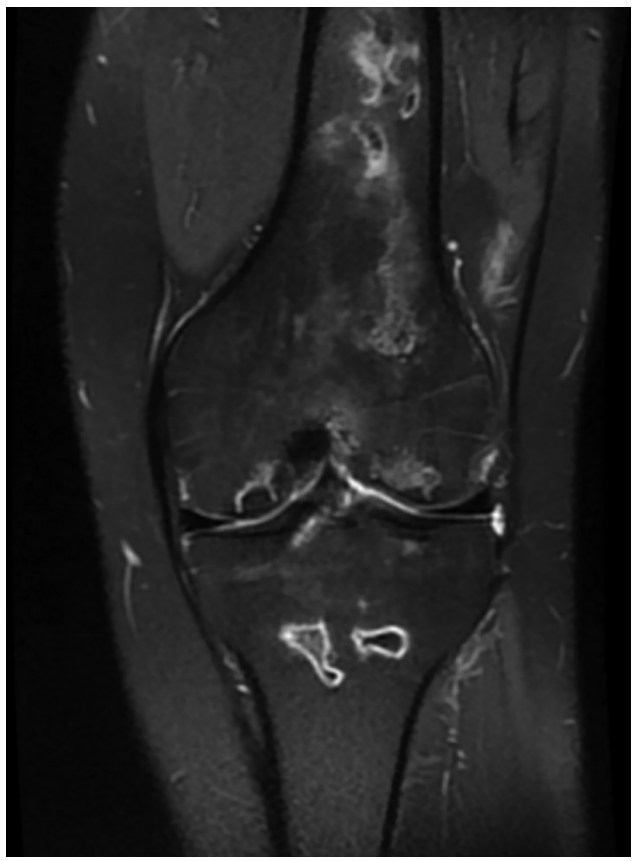

Fig. 6 – Coronal PDFS image of the left knee with extensive bone marrow oedema. PDFS, proton density fat saturated.

Discussion

ON, also termed ischemic, avascular or aseptic necrosis, is a condition associated with a variety of etiologies. Generally, ON is seen where there is direct vascular disruption, either by a traumatic insult, intravascular occlusion—seen in hemoglobinopathies and coagulopathies—or extravascular compression [1]. Since the 1990s ON has been increasingly described in HIV patients, with some studies suggesting a 100-fold increased risk as compared to the general population [2]. The mechanism by which ON occurs in these patients—whether as a direct result of the disease process, an adverse result of ART or via associated risk factors—remains unclear [3]. That HIV is an independent risk factor for ON is a controversial theory [4,5]. Popular hypotheses for this process suggest that higher titres of autoantibodies such as antiphospholipid and anticardiolipin antibodies, as seen in HIV patients, increase the risk of ON as this has been demonstrated in patients with systemic lupus erythematosus and antiphospholipid syndrome [6,7]. More convincing is the impact of pharmacological therapies used in HIV patients. ARTs have not been shown to cause ON directly, however their metabolic side effects, particularly hyperlipidemia and lipodystrophy, have been shown to increase risk [8,9]. It is well established that corticosteroids are an independent risk factor for ON and, owing to the various comorbidities HIV patients suffer, corticosteroids are commonly used in management [10–13]. Other regularly prescribed medications such as lipid-lowering drugs, testosterone, and megestrol acetate have each demonstrated an increase of ON in HIV patients [14,15]. Bisphosphonates are used for the management of bone disorders in HIV patients. They have been shown to cause ON, particularly in patients with hematological or breast malignancies, however there is little data specific to patients with HIV [10,11]. Lifestyle factors such as alcohol and smoking are also independent risk factors for ON and may also play a role in these patients [8]. The true burden of ON in HIV patients is not clear, particularly as studies have shown many incidents of asymptomatic ON in this group [2]. It has been reported to affect multiple sites in over two-thirds of cases, and is most frequently identified in the hip joint, second the knee and third the shoulder joint [12,13]. Studies assessing whether the immune status, or severity of HIV, impacts the development of ON have produced mixed results with some stating that patients with prior AIDS-defining illnesses are at increased risk of ON while others describe ON in patients with higher CD4 nadir counts [5,16]. Limited data describe the effect of viral load.

Although increasingly described in the literature there are currently no available guidelines to support the diagnosis and management of ON in HIV patients. The case in question describes a patient's journey between clinical specialists, in the absence of a predetermined pathway. As the case highlights, there is significant morbidity associated with ON and so timely identification and treatment is essential in improving patient's outcomes. It is therefore important to raise the profile of this issue in order to set up effective referral pathways and guidelines for management, locally and nationally.

Key take home messages

- Clinicians should have a high index of suspicion for ON in HIV patients presenting with joint pain.
- The identification of ON should prompt HIV testing in patients where the presence of ON cannot otherwise be explained.
- In individuals with HIV, ON tends to effect multiple joints and therefore there should be a low threshold to investigate ON at other sites, particularly as there is a high incidence of asymptomatic ON in the HIV population.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2018.10.032.

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